

IN THE SPECIFICATION:

Please amend the specification as follows:

At page 2, in the second full paragraph, please substitute the following section to provide the correct spelling of “titanium:”

--Besides the composite material implants are described consisting of layers, where the lower layer of the implant, often comprising metal or alloys like ~~titan~~ titanium or ~~titan~~ titanium alloy (WO 98/43550; WO 00/72777) is coated with a layer of the calcium phosphates (EP 0478532). Typically the coating with calcium phosphates is achieved by hydrothermal treatment (EP 0548365) or by soaking and precipitation (US-Patent 6,129,928, WO 97/41273) or plasma spraying (US-Patent 5,697,997, US-Patent 6,113,993, EP 0548365, EP 0739191, Lichtinger, 2001).--

At page 3, in the last paragraph, please substitute the following section to provide the correct spelling of “titanium:”

--A further method to overcome the quick outwash of the protein is described by Lichtinger et al. (2001) who treat the ~~titan~~ titanium alloy surface with chromosulfuric acid in order to achieve an ultrahydrophilic bioadhesive surfaces.—

At page 5, in the first full paragraph, please substitute the following section to provide the correct spelling of “titanium:”

--These prostheses are, preferably, formed from or coated with metallic surfaces as will be described in more detail below. Prostheses are made from titan or ~~titan~~ titanium alloys like titan alloy or stainless steel.--

At page 8, in the second full paragraph, please substitute the following section to provide the correct spelling of “titanium:”

--Many methods are described for the stabilization of proteins in pharmaceutical products. However, the experiments underlying this invention demonstrated that the well known techniques of protein stabilisation in liquid or freeze dried protein formulations can not be directly adapted to the adsorbed protein onto a metal surface. The coating of proteins onto metal

surfaces e.g. ~~titan~~ titanium or ~~titan~~ titanium alloys according to the methods disclosed in the state of the art referred to supra cause the occurrence of modified species of the protein which result in aggregation or oxidation of the proteins (for details see Example 5).—

At page 9, in the fourth full paragraph, please substitute the following section to provide the correct spelling of “titanium:”

--More preferably, the ~~titan~~ titanium alloy is a ~~titan~~ titanium alloy containing at least 50 % ~~titan~~ titanium. Furthermore preferably, said titan alloy is a Ti-Al-V-alloy, a Ti-Al-Fe alloy, a Ti-Al-Nb-alloy or a Ti-Mo-Zr-Al-alloy, most preferably Ti6Al4V.--

At page 22, in the description for Figures 6 and 7, please substitute the following description to provide the correct spelling of “titanium:”

--**Figure 6:** Release of rhGDF-5 from pretreated ~~titan~~ titanium surfaces. Summary of the results as determined by ELISA.

Figure 7: Coating of ~~titan~~ titanium surfaces with rhGDF-5 solution with and without sucrose.--

At page 24, in Example 5, please substitute the following section to provide the correct spelling of “titanium:”

--rhGDF-5 may be oxidized to a significant extent after the coating – release cycle using ~~titan~~ titanium sheets as surface. Here we describe a method and a device for coating avoiding protein oxidation during the coating procedure.

Device for coating ~~titan~~ titanium or ~~titan~~ titanium alloy with bone growth factor:

The coating process is performed under an inert gas atmosphere to exclude oxygen. To maintain these conditions a chamber is used. The chamber consists of a hermetically closed room with a continuous stream of inert gas, e.g. N₂ gas. Inside the chamber a slight excess pressure is maintained. The materials needed for the coating process are transported into the chamber through a gas tight lock. The chamber allows a manually as well as an automated coating process. For the definition and standardization of the coating process the relative humidity in the chamber is monitored and adjusted.

Coating:

The titan sheets were cleaned, washed with demineralized water and dried. The ~~titan~~ titanium sheets were coated with 60 µg of rhGDF-5. Each sheet was laid down flat in a dish and coated with rhGDF-5 solution on one side of the metal sheet.--

At page 25, immediately following Table 1, please substitute the following section to provide the correct spelling of "titanium:"

--The parameters tested in the experiments here have an influence on the amount of oxidized rhGDF-5 after extraction from the ~~titan~~ titanium sheets: Samples coated in the presence of air oxygen at room temperature reveal an amount of oxidized rhGDF-5 of 10.0 % ± 1.6 % as displayed in table 1 and figure 1.

At page 26, lines 1-2, please substitute the following section to provide the correct spelling of "titanium:"

--Example 6: Determination of the homogeneity of the coating of bone growth factor on ~~titan~~ titanium surfaces by fluorescence microscopy--

At page 27, for Example 7, please substitute the following section to provide the correct spelling of "titanium:"

--Example 7: Long term in vitro release of bone growth factor from pretreated ~~titan~~ titanium surfaces

We developed a method for coating bone growth factor on ~~titan~~ titanium surfaces. After standardized extraction we are able to analyze the protein for aggregates (Example 3), the amount of oxidized bone growth factor (Example 4) and are able to quantify the extracted protein (Example 1). In the experiment described here we determined the release kinetics of bone growth factor by incubation of coated ~~titan~~ titanium sheets in cell culture medium for 30 days. To mimic physiological conditions and metabolic activity, we exchanged the medium every 48h and quantified the amount of released protein by ELISA.--

At page 28, for Example 8, please substitute the following section to provide the correct spelling of "titanium:"

--Example 8: Coating and extraction of ~~titan~~ titanium or ~~titan~~ titanium alloy with rhBMP-2--

At page 29, for Example 9, please substitute the following section to provide the correct spelling of "titanium:"

--Example 9: Coating of ~~titan~~ titanium or ~~tit-titan~~ titanium an alloy with bone growth factor in the presence of sucrose

Here we describe the coating of ~~titan~~ titanium surfaces with rhGDF-5 solution with 10% sucrose. In comparison we coated titan surfaces with bone growth factor in 10 mmol/l HCl.--

At page 30, in the second and third paragraphs, please substitute the following section to provide the correct spelling of "titanium:"

--Subsequently the ~~titan~~ titanium material was washed in PBS for 1h at room temperature. Then the protein was extracted by incubation in 100 mmol/l HCl for 3 h at room temperature. The protein content of all solutions was determined by RP-HPLC quantification. Before quantification the PBS solution was adjusted to pH 2 to increase the solubility of bone growth factor.

In the experiments described herein, two different coated metal pieces were prepared:

~~Titan~~ Titanium sheets coated with bone growth factor solutions with or without 10% sucrose.

The results of the coating and extraction procedure are summarized in Table 4:--